PCDDs, PCDFs, and PCBs in Human Blood in Relation to Consumption of Crabs from a Contaminated Fjord Area in Norway

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Consumption of fish and shellfish from contaminated areas may be an important source of human exposure to persistent organohalogen compounds such as polychlorinated biphenyls (PCBs), polychlorinated dibenzo-*p*-dioxins (PCDDs), and polychlorinated dibenzofurans (PCDFs). We determined concentrations of 2,3,7,8-substituted PCDDs and PCDFs and 19 PCB congeners in whole blood samples from three groups of men, 40–54 years of age, with different consumption levels of crabs from a fjord area in southern Norway polluted with organochlorine compounds from a magnesium production plant. A significant increase of many PCDD/PCDF congeners was found in the blood when comparing the referents, moderate-, and high-intake groups. The greatest difference was observed for several of the PCDFs that are characteristic for the contamination of the marine biota of the fjord. PCBs, in general, play a minor role in the contamination of the fjord by the magnesium production process, except for the highly chlorinated congeners such as PCB-209. Nevertheless, almost all PCBs increased from the referents to the high-intake group. However, the relative concentrations of several highly chlorinated PCBs (particularly PCB-209) in blood are unexpectedly low compared to their abundance in crabs, indicating low uptake of these congeners. The exposure to PCDDs/PCDFs from crab consumption calculated from individual body burdens of these compounds were in good agreement with the intake estimated from previously measured concentrations in crabs, reported fishing sites, and consumption. Almost all subjects in the high-intake group exceeded the tolerable weekly intake of 35 pg TEQ/kg body weight/week proposed by a Nordic Expert Group. *Key words:* blood, crab consumption, polychlorinated biphenyls, polychlorinated dibenzofurans, polychlorinated dibenzo-*p*-dioxins, . *Environ Health Perspect* 104:756–764 (1996)

A magnesium factory, situated in the inner part of the Frierfjord in southern Norway, produces considerable amounts of organochlorine compounds such as polychlorinated biphenyls (PCBs), polychlorinated dibenzo-*p*-dioxins (PCDDs), and polychlorinated dibenzofurans (PCDFs) during the production of metallic magnesium (Fig. 1). As much as 50–100 kg TCDD toxic equivalents (TEQs) may have been discharged to the Frierfjord during the past 35 years (*1*). As part of the National Program on Pollution Monitoring, PCDDs/PCDFs, PCBs, and non-*ortho*-PCBs have been monitored in sediments and marine organisms at various distances from the source since 1986, 1989–1990, and 1992, respectively (*2–4*). In spite of a reduction in the emissions of organochlorine compounds by more than 98% from 1990 to 1992 (*1*), considerable amounts of PCDDs and PCDFs are still observed in most marine organisms of the area. Restrictions on commercial fishing and recommendations to the general public to reduce consumption of fish and shellfish have been established for the contaminated fjord area. However, the area is popular for recreational purposes, and some residents still catch and consume considerable amounts of local fish and shellfish. Particularly during the summer and autumn, the crab species *Cancer pagurus* is a popular food item in this area. These crabs contain high concentrations of organochlorine compounds, revealing the characteristic isomer pattern of the magnesium process (*5*) with tetra- to hexa-CDFs being the predominant PCDD/PCDF congeners and decachlorobiphenyl (PCB-209) the most abundant PCB congener.

PCDDs, PCDFs, and PCBs are complex mixtures of persistent lipophilic substances and tend to accumulate in marine and terrestrial food chains. The general population is mainly exposed to these substances through fatty food, leading to a background body burden of these substances (*6–8*). People consuming large amounts of contaminated seafood may have elevated concentrations of organochlorine compounds in their tissues compared to the general population (*9–14*). Due to low biodegradation and excretion in humans, these substances accumulate in the body fat, and their concentrations reflect external exposure (*6–8,15,16*). Cumulative exposure has been assessed by analyzing adipose tissue, human milk, and/or blood (*17–20*).

The patterns of PCDDs, PCDFs, and PCBs in humans do not directly reflect the patterns of discharge to the environment owing to differences in physical properties, e.g., lipophilicity and volatility, and biodegradability of the individual compounds in the food chain. Of the PCDD/PCDF congeners, the 2,3,7,8-substituted PCDD and PCDF congeners are the most resistant to metabolism and are generally the only congeners found in human tissue (*7,8*). The hepta- and octa-CDD congeners are by far the most abundant in samples from the general population (*8*). In contrast, fish and other organisms from the aquatic environment usually contain quite low concentrations of these congeners (*21,22*).

For risk assessment purposes and to assist in risk management, the concept of toxic equivalency factors (TEFs) for the 2,3,7,8-substituted congeners has been developed to express the toxic potency of complex mixtures of PCDDs/PCDFs in biological samples by a single value, the 2,3,7,8-TCDD toxic equivalent (TEQ) (*23,24*). In addition, several of the non-, mono-, and di-*ortho*-substituted PCBs, which induce effects similar to those caused by PCDDs and PCDFs, have been given provisional TEF values (*25*). Even though the application of the proposed TEFs to health risk assessment has been criticized, particularly for the PCBs (*26*), they are widely used for risk management.

The objective of the present study was to assess the role of consumption of crabs from the contaminated fjord area for the exposure to PCBs, PCDDs, and PCDFs. We therefore determined blood concentrations of these compounds in 24 male crab consumers and 10 referents and recorded information on crab consumption and fishing site as well as consumption of fish and other food items to answer the following questions: 1) Does the consumption of crabs from the Frierfjord area lead to increased body burdens of PCDD/PCDF

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and PCB compounds? 2) Are the patterns for PCDDs/PCDFs and PCBs found in human blood changed by the exposure through crab consumption? 3) Do exposure estimates based on measured blood concentrations agree with those based on reported crab intake? 4) What is the individual exposure level compared to present recommended tolerable intake of toxic equivalents?

Materials and Methods

Study group and sample collection. It is well documented that the body burden of PCDD/PCDF and PCB compounds increases with age and for women decreases with the number of breastfed children (*7,18,27*). To avoid variation of body burden with age and sex, we restricted the study to male subjects in a relatively close age range. The study was approved by the Regional Committee of Medical Research Ethics, and informed consent was obtained from all participants. A total of 34 male volunteers, age 40–54 years, participated in the study. All subjects were living in the Frierfjord area of Norway. Male crab consumers (high and moderate intake) were recruited nonrandomly through announcements in the newspapers and other media. Of the 24 crab consumers, 20 had eaten crabs for more than 10 years, 2 for 5–10 years, and 2 did not report the duration of crab consumption. The male referents were drawn randomly from the Register of Population. Blood was sampled after overnight fasting. About 250 ml venous blood was drawn from each subject into thoroughly cleaned glass bottles (Duran, Schott, Germany) and kept frozen at -20°C until analyzed. A questionnaire including information on crab and fish consumption, intake of other fatty food items, and other relevant factors was completed by each donor. All subjects reported being healthy. Information concerning the subjects of the three groups is summarized in Table 1.

Standards and chemicals. Acetone was glass-distilled grade and all the other organic solvents were pestiscan grade from Labscan (Dublin, Ireland) or Merck (Darmstadt, Germany). Sulfuric acid (Scanpure, 98.3%) and nitric acid (Scanpure, 65%) were purchased from Chem Scan A/S (Elverum, Norway). The $^{13}C_{12}$-labeled PCB-77, PCB-126, PCB-169, and 2,3,7,8-substituted PCDDs and PCDFs as well as the native PCDDs and PCDFs and ^{37}Cl-2,3,7,8-TCDD were from Cambridge Isotope Laboratories (Woburn, Massachusetts). The normal PCB standards were purchased from Cambridge Isotope Laboratories or from Restek (Sulzbach, Germany). Silica gel, aluminum oxide, sodium sulfate, and potassium hydroxide were from Merck and the activated carbon AX-21 was from Anderson Development Company (Adrian, Michigan). All adsorbents were prepared as previously described by Smith et al. (*28*) and Oehme et al. (*21*). All glassware for organochlorine analysis was washed in 2.5% RBS detergent and distilled water, then heated in an oven at 500°C overnight.

Determination of PCDDs, PCDFs, and non-ortho PCBs. The extraction was performed after a method described by Päpke et al. (*29*). We packed 100 g of Hydromatrix (plankton marine diatomite; Varian Sample Preparation Products, Harbor City, California) and 50 g of sodium chloride in alternating layers into glass columns (30 cm × 5 cm i.d.). Thereafter, the adsorbents were washed with 375 ml of *n*-heptane/isopropanol (3:2, v/v) and 375 ml of methylene chloride and dried at 50°C overnight. We transferred 45–50 g of whole blood, spiked with internal standards and diluted with water and ethanol (1:0.66:0.13, v/v/v) to the column. The extraction was performed by eluting with 650 ml of *n*-heptane/isopropanol (3:2, v/v). The eluate was concentrated under a gentle stream of purified nitrogen and dissolved in about 2 ml of cyclohexane. The extract was transferred to glass columns (10 cm × 2 cm i.d.) filled with sodium sulfate for removal of any precipitated salt and evaporated to dryness with a gentle stream of nitrogen before gravimetric determination of the lipids.

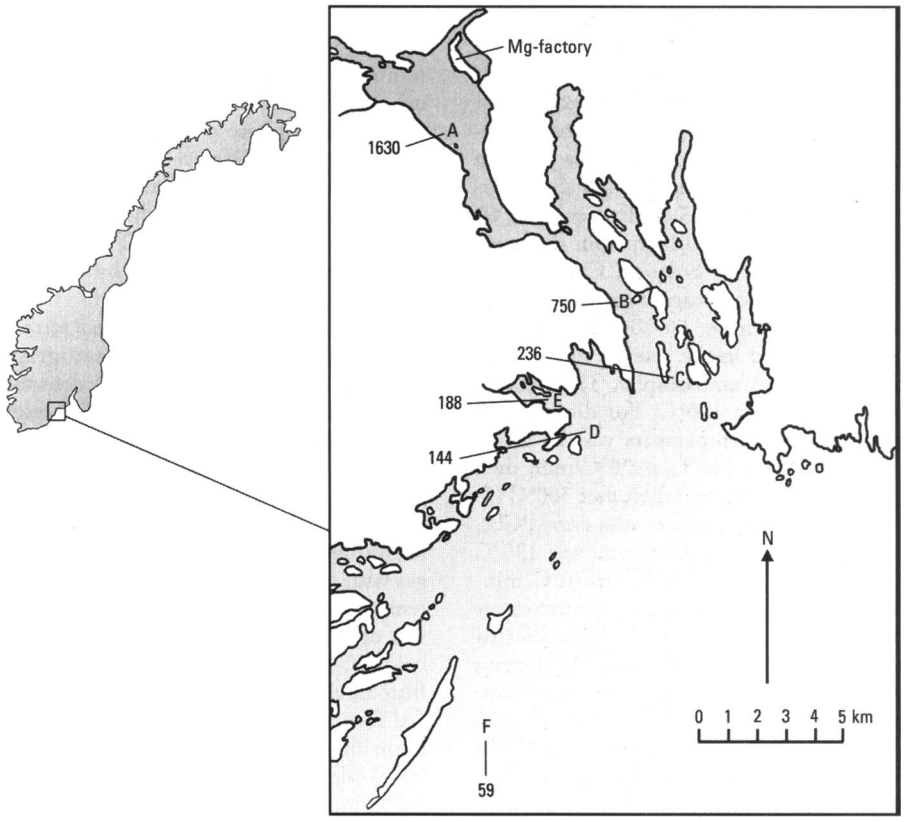

Figure 1. Map of Norway and the Frierfjord fjord area, with concentrations of PCDDs/PCDFs (pg TEQ/g wet weight) in crab hepatopancreas obtained during the National Program on Pollution Monitoring 1992 (*3*) at the regular sampling sites A to F.

Table 1. Mean and range of age, body mass index (BMI), crab and fish consumption, % fat in the blood samples, and polyunsaturated fatty acids (PUFA) in serum phosphatidylcholine for the three groups

	Referents (*n* = 10)	Moderate intake (*n* = 15)	High intake (*n* = 9)
Age (years)	46.7 (41–50)	45.33 (40–54)	46.22 (41–52)
BMI (kg/m^2)	25.4 (22.2–30.7)	26.2 (21.7–32.7)	27.3 (21.5–30.9)
Crab intake (no./year)	0	11.9 (10–38)	77.2 (40–150)
Crab equivalents (no./year)	0	19.6(10–115)	93.2 (24.8–156)
Fish intake (meals per week)	1.1 (0.5–2.5)	1.4 (0.25–2.5)	1.8 (0.5–3.5)
Extracted fat from whole blood (weight %)	0.39 (0.29–0.48)	0.37 (0.28–0.55)	0.47 (0.33–0.69)
Σ*n*-3 PUFA (weight %)	11.72 (8.95–16. 01)	12.98 (8.3–20.46)	11.64 (8.66–15.5)
Σ*n*-6 PUFA (weight %)	35.25 (30.43–38.89)	34.31 (24.55–38.8)	35.88 (31.32–38.88)

The clean-up was carried out in a multicolumn system according to a slight modification of the method described by Smith et al. (*28*). In brief, the fat extract was passed through two columns in series using a total of 825 ml of dichloromethane/cyclohexane (1:1, v/v) followed by 50 ml of dichloromethane/methanol/benzene (15:4:1, v/v/v). The first column contained sodium sulfate, potassium silicate, and silica gel, and the second contained activated carbon (AX-21) dispersed on glass fibers. PCDDs and PCDFs were removed from the carbon column by reversed elution with 100 ml of toluene. The crude dioxin fraction was further purified by chromatography using two Pasteur pipettes in series filled with acidic silica and basic alumina, respectively. ^{37}Cl-2,3,7,8-TCDD was added to the final extract as a recovery control standard and 10 µl of *n*-nonane as a keeper before concentrating to about 15 µl.

The GC-HRMS instrument consisted of a VG AutoSpec high-resolution mass spectrometer with Opus Quan software program and a Hewlett Packard 5890 gas chromatograph with a DB-5 MS capillary column, 60 m × 0.25 mm i.d., 0.1-µm film thickness (J&W Scientific, Folsom, California). Helium was used as carrier gas with a linear velocity of 28 cm/sec (at 200°C). Injections were performed in the splitless mode using an HP 7673 A autosampler. The injector temperature was 280°C. For dioxins, the initial column temperature was 90°C (1-min hold), then 197°C at 20°C/min, then 250°C at 2°C/min, and thereafter 300°C (5-min hold) at 5°C/min. For non-*ortho*-PCBs, the initial column temperature was 130°C (1-min hold), then 200°C at 20°C/min, then 212°C at 0.6°C/min, and thereafter 300°C (10-min hold) at 5°C/min. Selected ion detection was carried out in the electron impact mode with an MS ion source temperature of 250°C, an electron energy of 35 eV, and a resolution of 10,000 and 9,000 for the dioxins and the non-*ortho*-PCBs, respectively. Dwell time for each ion was 80 msec. Perfluorokerosene was used to provide suitable lock masses. The transfer line was held at 280°C.

Quantitation. ^{13}C-labeled analogues of the 2,3,7,8-substituted PCDDs and PCDFs, except OCDF, were added as internal standards before extraction of samples. ^{37}Cl-2,3,7,8-TCDD was added to the final extract as a recovery control standard. Multilevel calibration was performed. Detection limits were 0.5–8 pg/g fat, depending on the congener. Recoveries of the internal standards were between 70 and 100%.

For non-*ortho*-PCBs, ^{13}C-labeled analogues were used as internal standards. Multilevel calibration was performed before or directly after each analysis series. PCB-189 was added to the final extract to measure the recovery of the ^{13}C-labeled standards. Detection limits were 1–7 pg/g fat for different congeners and sampling conditions. Recoveries were between 50 and 80%. PCB-77 could not be quantitated due to coelution with contaminants. However, this non-*ortho*-substituted PCB does not contribute significantly to the dioxin-related toxicity as both the concentration in human samples is generally low (*16,19*), and its WHO-TEF value is very small.

Determination of PCBs. Mono- and multi-*ortho*-PCBs were extracted from 15 ml of whole blood by the same extraction procedures as the PCDDs and PCDFs and the non-*ortho*-PCBs. The lipid extracts were dissolved in cyclohexane (about 0.1 g lipid/ml) and treated twice with an equal volume of concentrated sulfuric acid to remove the major part of the lipids and other interfering organic compounds. The sulfuric acid phase was reextracted with cyclohexane. Additional purification was performed by chromatography on basic alumina using hexane/dichloromethane (80/20, v/v) as an eluent. The organic phase was reduced to 1 ml by a gentle stream of purified nitrogen.

GC analysis was performed with a Perkin Elmer 8700 gas chromatograph equipped with an electron capture detector, an AS-8300 autosampler and a PE Nelson Model 1020 personal integrator (Perkin-Elmer Corp., Beaconsfield, UK). Hydrogen was used as carrier gas with a linear velocity of 28 cm/sec (at 100°C). Argon/methane (5%) was used as make-up gas with a flow rate of 50 ml/min. Injector temperature was 270°C and the detector was operated at 330°C. A DB-5 capillary column, 50 m × 0.25 mm i.d., 0.25 µm film thickness (J&W Scientific, Folsom, California) was temperature-programmed from 60°C (1-min hold) to 200°C at 20°C/min, then to 280°C (10-min hold) at 2.0°C/min.

PCB-116 was used as an internal standard for the mono-*ortho* and multi-*ortho* PCB congeners (IUPAC nos. 28, 52, 74, 99, 105, 118, 128, 138, 153, 156, 157, 170, 180, 187, 194, 206, 209). Detection limits for the multi-*ortho*- and mono-*ortho*-substituted PCBs were 0.01 to 0.05 ng/g fat, depending on the congener.

Toxic equivalency factors. Concentrations expressed in 2,3,7,8-TCDD toxic equivalents (TEQs) were calculated according to a model proposed by a Nordic expert group (*30*) for PCDDs/PCDFs and by an expert group convened by the World Health Organization (WHO) (*25*) for the PCBs. The Nordic model differs from the international TEFs (*31*) in that the TEF for 1,2,3,7,8-penta-CDF is 0.01 (i.e., a factor of 5 lower than in the international model).

Quality assurance of organochlorine compound analysis. All samples were analyzed coded. For each set of five samples, a method blank was prepared using the same extraction and preparation procedures. New glass columns and adsorbents were used for each sample to avoid cross-contamination. For PCDDs/PCDFs, most blank samples contained less than 1 pg of all analytes, except for the ubiquitous octachlorodibenzo-*p*-dioxin (OCDD). The repeatibility of the entire method, the recovery rates of isotopically labeled internal standards, and the detection limit for the method were in good agreement with those values reported by Päpke et al. (*29*), who used the method successfully in WHO interlaboratory control studies.

For PCBs, recovery rates for all quantitated congeners throughout the procedure were in the range of 45–80%. Good analytical quality for determination of PCBs in fish oil and of PCDDs/PCDFs in human milk was confirmed by successful participation in interlaboratory quality control studies organized by the Swedish Environmental Protection Agency in 1991 and by WHO/EURO in 1991–1992, respectively.

Determination of fatty acids. We allowed 10 ml of venous blood to clot and immediately separated serum by centrifugation, cooled it, and froze it within 6 hours at -70°C until analysis. The concentration of fatty acids in plasma phospholipids was measured essentially as described elsewhere (*32*). Briefly, plasma lipids were extracted with *n*-butanol (*33*) and phosholipids were isolated from the lipid extracts by column chromatography on Sep-Pak C_{18} cartridges (Waters Corp., Milford, Massachusetts). Diheptadecanoylglycerophosphocholine and butylated hydroxytoluene were added as internal standard and antioxidant, respectively. Phospholipids were transmethylated and quantitated by gas chromatography (*34*). A reference human serum sample was included as a control to monitor analytical performance. The day-to-day coefficient of variation for 20:4 (*n*-6), 20:5 (*n*-3), and 22:6 (*n*-3) fatty acids were 3.8, 3.7, and 4.7%, respectively. The results were quantitated as milligrams of phospholipid fatty acid per liter of serum.

Statistical analysis. Nonparametric tests were chosen for statistical analysis because lack of normality was found in several distributions of PCB, PCDD, and PCDF concentrations. The Mann-Whitney *U*-test in the statistical program Statview SE (Abacus Concepts, Inc.

Berkeley, California) was used to compare groups. Significant difference was set at $p < 0.05$. Correlations were calculated using the Pearson correlation coefficients.

Results

The crab consumers were divided into two groups, a moderate-intake group (10–38 crabs per year) and a high-intake group (>40 crabs per year). These two groups and referents were compared with respect to age, body mass index, fish intake, fat in whole blood, and relative levels of 22:5 (*n*-6) polyunsaturated fatty acids (PUFA), total *n*-3 PUFA, and total *n*-6 PUFA in blood (Table 1). In addition to differences in crab intake, there was a slight nonsignificant increase in the intake of fish, particurlarly for the high consumers of crabs. There were no differences with respect to consumption of milk and dairy products or other sources of animal fat. There was no other significant difference in age of the subjects, ranging from 40 to 54 years, and no correlation between the age and the level of PCDDs and PCDFs in blood was observed.

In addition to the the number of crabs eaten, exposure to organochlorine compounds (OCs) is highly dependent on the location of the fishing sites and which parts of the crabs are consumed. The hepatopancreas of the crab has a high fat content (about 15–20%) compared to the rest of the crab meat and accordingly contains most of the OCs. All but two of the subjects in our study group reported eating whole crabs, including the hepatopancreas.

There was a considerable decrease (about 25 times) of PCDD/PCDF in crab hepatopancreas from the inner part of the fjord (site A), close to the magnesium factory, to sampling site F, about 35 km from the source (Fig. 1). To account for this gradient in organochlorine content of crabs as a function of distance from the source, we introduced equivalency factors according to the relative PCDD/PCDF content of the crab hepatopancreas. These factors ranged from 10 at site A (corresponding to 1630 pg TEQ/g wet weight) to 0.36 at site F (corresponding to 59 pg TEQ/g wet weight). The reported number of crabs consumed was then multiplied with the factors closest to the reported fishing sites. In cases where the fishing sites were at approximately equal distances from two monitoring sites, interpolated factors were used. Crab equivalents consumed per year in the different groups are given in Table 1.

Concentrations of 17 2,3,7,8-substituted PCDDs and PCDFs, given as mean, median, and ranges, divided into three groups according to the reported crab intake, are listed in Table 2. Blood concentrations for many PCDD and PCDF congeners in crab consumers are significantly raised compared to the referents, particularly for the penta- and hexa-CDFs. The most pronounced difference between the control and high-intake groups (more than 14 times) was observed for 1,2,3,4,7,8-hexa-CDF. There was also a significant increase in the level of several PCDDs, mostly the lower-chlorinated ones. In contrast, the concentrations of hepta- and octa-CDDs tended to decrease from the control to the high-intake group, but not significantly.

In Figure 2, the profile of 2,3,7,8-substituted congeners in crab hepatopancreas is compared with concentrations found in the blood from persons with no and high crab consumption. The PCDD/PCDF profile in the high-intake group is clearly influenced by the profile found in crab hepatopancreas. The PCDD profiles of the blood samples from both the high-intake group and the referents are dominated by octa-CDD which contributes little to the sum of PCDDs/PCDFs in crab hepatopancreas; however, this congener is clearly less dominant in the crab eaters.

When plotting blood concentrations of individual congeners against the intake of crab equivalents, good linear correlations (*r*

Table 2. Mean, (median), and range of PCDDs and PCDFs congeners in blood samples for the three groups of men with different crab intake[a]

Congener	Referents (*n* = 10)	Moderate intake (*n* = 15)	High intake (*n* = 9)
2,3,7,8-TCDD	3.6 (3.1)* 0.2–7.0	7.7 (6.8) 3–13.6	11.0 (9.2) 6.3–22.4
1,2,3,7,8-PeCDD	5.9 (5.6)* 0.5–10.6	17.3 (15.0)** 6.9–34.8	28.3 (24.8) 15.4–45.13
1,2,3,4,7,8-HxCDD	2.4 (2.2)* 0.9–3.4	8.0 (6.3) ND–30.1	10.8 (11.4) 4.0–17.4
1,2,3,6,7,8-HxCDD	14.7 (14.2)* 2.7–24.5	27.6 (24.8) 13.1–48.2	39.1 (34.4) 16.9–63.7
1,2,3,7,8,9-HxCDD	4.3 (3.8) 0.6–7.3	8.6 (6.7) ND–43.5	9.9 (8.8) 5.9–20.9
1,2,3,4,6,7,8-HpCDD	54.1 (34.7) 10.0–179.1	45.5 (39.8) 20.8–77.4	33.3 (31.1) 16.9–63.7
1,2,3,4,6,7,8,9-OCDD	477.9 (470.3) 51.7–951.1	335.6 (350.9) 157.1–440.4	266.8 (284.9) 104.2–362.9
ΣPCDDs	562.8 (532.5)	450.3 (450.3)	399.3 (404.6)
PCDDs, Nordic-TEQs	9.7 (8.7)	21.5 (18.8)	31.8 (27.7)
2,3,7,8-TCDF	2.8 (2.9) 0.6–5.0	5.1 (4.1) ND–12.7	7.2 (6.4) 1.7–16.5
1,2,3,7,8,-PeCDF	1.8 (1.6)* 0–10.9	7.2 (6.3) 1.5–19.5	13.4 (13.3) 1.29–34.59
2,3,4,7,8-PeCDF	17.1 (15.5)* 4.9–33.5	54.0 (52.8)** 17.6–111.9	102.2 (103.6) 51.5–147.8
1,2,3,4,7,8-HxCDF	8.7 (7.4)* 1.9–21.4	54.9 (55.2)** 10.8–107.1	130.1 (130.2) 34.3–232.6
1,2,3,6,7,8-HxCDF	9.7 (7.7)* 2.3–21.9	44.8 (46.9)** 8.8–90.3	102.7 (77.8) 26.6–217.1
2,3,4,6,7,8-HxCDF	4.3 (3.8)* 1.6–6.7	8.9 (7.9) ND–33.0	14.3 (10.9) 3.2–29.4
1,2,3,7,8,9-HxCDF	0.9 (0.9)* 0–1.0	3.6 (1.1) ND–34.3	2.3 (2.0) 0–5.4
1,2,3,4,6,7,8-HpCDF	18.0 (13.3) 2.5–53.3	44.3 (46.8)** 0.1–117.5	93.0 (92.6) 26.8–201.2
1,2,3,4,7,8,9-HpCDF	1.0 (1.1) ND–0.9	4.8 (1.5) ND–46.2	2.6 (2.4) ND–5.3
1,2,3,4,6,7,8,9-OCDF	8.6 (6.1) 1.3–30.0	13.4 (7.4) ND–93.9	5.4 (6.1) 2.1–8.8
ΣPCDFs	72.8 (60.2)	241.0 (230.1)	473.3 (446.3)
PCDFs, Nordic-TEQs	11.4 (10.2)	39.3 (38.5)	77.9 (75.7)
ΣPCDDs/PCDFs	631.1 (589.4)	691.3 (680.4)	872.5 (850.9)
PCDDs/PCDFs, Nordic-TEQs	21.1 (18.9)	60.8 (57.3)	109.6 (103.4)

ND, not dectected.
[a]Concentrations are given in pg/g fat.
*Significantly different as compared with the moderate-intake group ($p<0.05$ by Mann-Whitney U-test).
**Significantly different as compared with the high-intake group ($p<0.05$ by Mann-Whitney U-test).

>0.6) were obtained for 2,3,4,7,8-penta-CDF, 1,2,3,4,7,8-hexa-CDF, and 1,2,3,6,7,8-hexa-CDF, as well as TCDD and penta-CDD. The correlations were lower (r = 0.4–0.6) for 2,3,7,8-tetra-CDF, 1,2,3,7,8-penta-CDF, 1,2,3,4,7,8-hexa-CDF and 2,3,4,6,7,8-hexa-CDF (not shown).

Mean, median, and ranges of blood concentrations of 2 non-*ortho*-PCBs, 4 mono-*ortho*-PCBs, and 13 other PCBs for the three study groups are given in Table 3. Almost all PCB congeners increased slightly from the referents to the high-intake group with significant increases for PCB-99, 128, 156, 157, 170, 180, 194, 206, and 209. However, no significant correlation was observed between the concentrations of sum PCBs (dominated by PCB-138, 153, 170, and 180) and crab intake (r = 0.19).

A comparison of the PCB profiles in crab hepatopancreas (*3*) from the Frierfjord area and in blood samples of the referents and the high-intake group is shown in Figure 3. There are only minor differences in the profiles for the referents and the high-intake group, and there is little agreement between the blood profiles and the profile found in crabs. The high concentration of PCB-209 found in crabs from the Frierfjord area is not reflected in the blood of the crab consumers.

The contribution of different dioxinlike compounds to the total TEQs for the three study groups is presented in Figure 4. While there is only a slight increase in TEQs for the PCBs with increasing crab consumption, the PCDD/PCDF-related TEQs are about five times higher in the high-intake group compared to the referents. Thus, the relative contribution of PCBs to the total TEQs drops from 65% in the referents to about 35% in the high-intake group.

When plotting the PCDD/PCDF-related TEQs in blood against the intake of crab equivalents, a good correlation was observed (Fig. 5, r = 0.75). When only numbers of crabs were used, the correlation factor was 0.68, and several of the data points for subjects who caught crabs close to extreme sites B and F (see Fig. 1) were remote from the regression line. This emphasizes the usefulness of crab equivalents, which accounts for the gradient in PCDD/PCDF concentrations of crabs as a function of the distance from the source.

Based on the measured blood concentrations, we wanted to estimate the total body burden of PCDDs /PCDFs, expressed as TEQs. We assumed that the whole dose is evenly distributed in the body fat compartment (*35–37*). The percentage of body fat was calculated from the body mass index

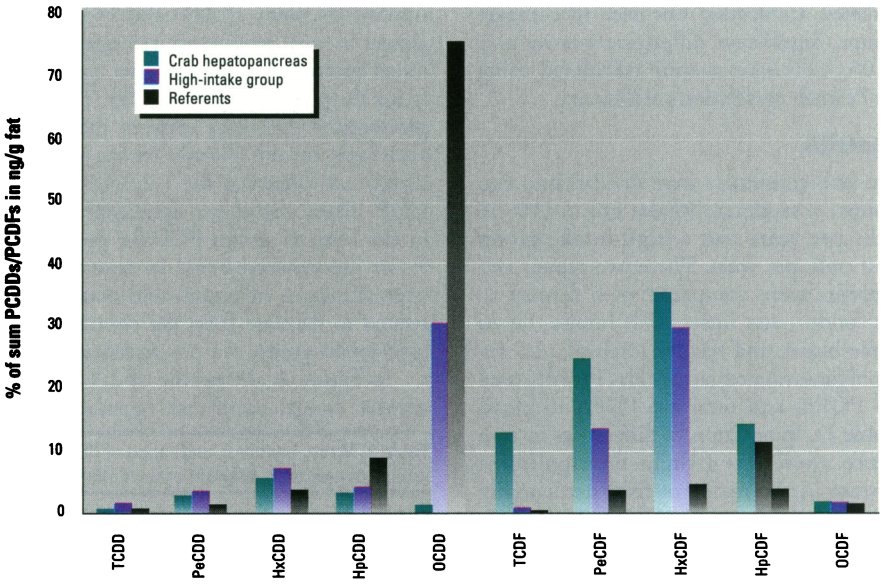

Figure 2. Profile of PCDDs/PCDFs in blood samples from referents and high-intake group compared to the profile in crab hepatopancreas from sampling site D.

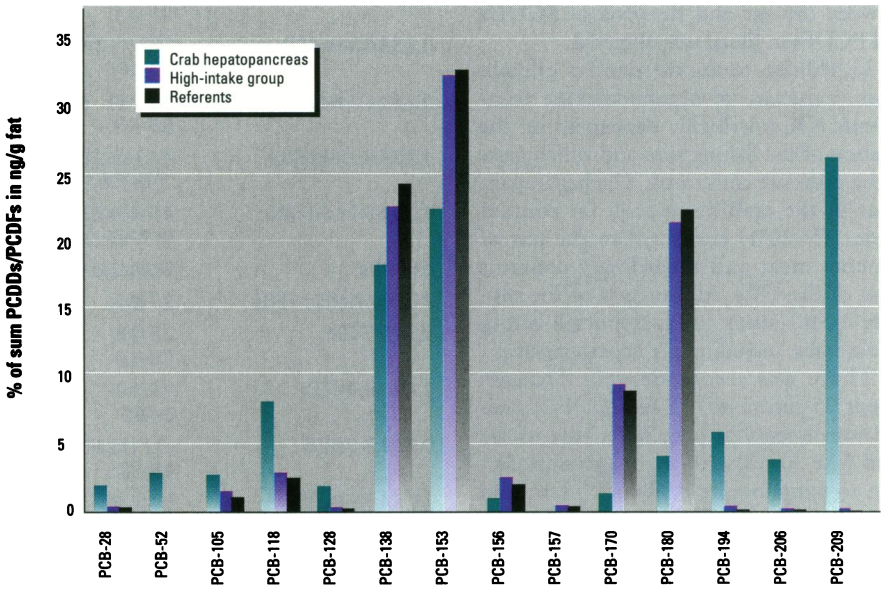

Figure 3. Profile of PCBs in blood samples from referents and high-intake group compared to the profile in crab hepatopancreas from sampling site D.

and age, according to an empirical equation developed by Deurenberg et al. (*38*). The mean body burdens and ranges for the referents, the moderate-intake group and the high-intake group were 5.2 (1.1–11.5), 15.5 (5.5–30.4), and 28.7 (12.7–45.9) ng/kg body weight, respectively. Based on these calculated body burdens, we wanted to estimate the average weekly intake. Several assumptions were made. Although the kinetics differ between the individual compounds (*39*), PCDD/PCDF concentrations were expressed as a single number, the TEQ. We use a single-compartment model with first-order kinetics. Several half-life values for 2,3,7,8-TCDD elimination have been reported varying from 3 to 11 years (*40,41*). We assumed an average half-life of 7 years and assumed that PCDD/PCDF concentrations in the subjects had reached a steady state. Assuming complete absorption, we used the following equation to calculate the mean weekly intake:

$$WI = C \times BF \times \left[\frac{\ln 2}{7(52\ \text{weeks})}\right]$$

where WI = weekly intake (pg/kg body weight/week), C = concentration of

Table 3. Mean, (median) and range of PCB congeners in blood samples for the three groups of men with different crab intake[a]

Congener	IUPAC no.	Referents (n = 10)	Moderate intake (n = 15)	High intake (n = 9)
2,4,4′	28	2.9 (3.3) 1–4.3	4.1 (4.8) 1.3–9.4	4.2 (3.2) 1.8–10.4
2,2′,5,5′	52	0.4 (0.5) ND–0.6	0.7 (0.6) ND–1.9	0.6 (0.6) ND–0.9
2,4,4′,5	74	14.1(15.5) 5.2–20.5	11.6 (12.3) 0.7–24.6	17.5 (18.3) 4.2–21.8
2,2′,4,4′,5	99	12.1 (11.1)* 4.5–18.2	12.1 (10.1) 3.8–21.8	16.1 (14.7) 5.1–23.9
2,2′,3,3′,4,4′	128	1.5 (1.4)* 1.1–2.8	1.5 (1.4) 0.3–2.8	3.7 (3.3) 1.9–6.8
2,2′,3,4,4′,5′	138	287.4 (223.9) 145.9–359.5	329.8 (289.2) 220.1–478.1	334.2 (299.1) 180.7–516.4
2,2′4,4′,5,5′	153	385.3 (361.9) 188.6–553.6	438.8 (390.3) 236.1–699.6	479.2 (417.3) 289.2–751.5
2,2′,3,3′,4,4′,5	170	105.5 (100.4)* 63.9–141.9	124.7 (116.7) 34.9–229.0	140.5 (133.4) 86.6–314.8
2,2′,3,4,4′,5,5′	180	264.3 (237.9)* 135.3–346.0	283.5 (256.5) 239.9–610.9	317.4 (315.9) 239.0–650.9
2,2′,3,4′,5,5′,6	187	34.1 (36.6) 5.6–25.4	39.8 (25.1) 1.4–38.9	46.8 (44.2) 8.0–29.2
2,2′,3,3′,4,4′,5,5′	194	1.6 (0.53)* ND–4.8	4.2 (4.3) ND–9.0	6.2 (5.6) 3.1–11.4
2,2′,3,3′,4,4′,5,5′,6	206	1.5 (1.4)* 0.3–0.9	3.6 (3.5) ND–11.9	3.2 (4.2) ND– 5.61
2,2′,3,3′,4,4′,5,5′,6,6′	209	0.9 (1.2)* 0–2.3	2.1(1.8) 1.4–4.7	3.4 (4.7) 1.2–9.9
2,3,3′,4,4′	105	11.7 (9.2) 1.9–19.9	17.5 (18.3) 4.3–49.8	21.9 (19.9) 11.7–41.9
2, 3′,4,4′,5	118	29.3 (32.2) 11.1–42.6	35.6 (34.2) 2.3–72.1	41.7 (39.2) 38.9–74.8
2,3,3′,4,4′,5	156	23.7 (26.2)* 8.7–34.6	31.5 (29.7) 6.7–46.3	37.4 (35.6) 22.3–53.7
2,3,3′,4,4′,5′	157	4.2 (4.4) 1.9–6.0	3.6 (3.5) 0.4–9.6	7.2 (6.5) 3.7–13.3
3,3′4,4′	77	NA	NA	NA
3,3′4,4′,5	126[b]	93.4 (100.7) 8.02–173.2	93.03 (92.6) 14.8–222	94.5 (98.1) 20.2–286.8
3,3′4,4′,5,5′	169[b]	70.1 (72.7) 4.9–108.9	94.7 (92.8) 18.3–199.1	119.6(89.7) 23.4–254.1
ΣPCBs	1180.6 (1067.8)	1344.2 (1202.5)	1481.4 (1365.9)	

ND, not detected.
[a]Concentrations are given in ng/g fat, if not stated otherwise.
[b]Value in pg/g fat.
*Significantly different as compared with the high-intake group (p<0.05 by Mann-Whitney U-test).
NA, not analyzed due to interfering compounds.

PCDD/PCDF in blood (pg/g fat), and BF = body fat fraction (g/kg body weight). It is obvious that this approach can only give a rough estimate of the weekly intake, particularly due to the assumption of a single half-life for all PCDD/PCDF congeners. Calculation of intake of PCDD/PCDF from measured blood levels gives for the referents a weekly intake of 9.7 (2–22) pg/kg body weight (mean and ranges), for the moderate-intake group 31 (10–61) pg TEQ/kg body weight, and for the high-intake group 62 (24–114) pg TEQ/kg body weight/week.

We further calculated the yearly intake of PCDDs/PCDFs from crab consumption using the differences between the blood concentrations of the individual crab consumers and mean blood concentrations of the referents. The values were 63–317 ng TEQ/year for the high-intake group and 2–244 ng TEQ/year for the moderate-intake group. These values were compared to estimates of yearly intakes based on previously measured concentrations in crabs, reported fishing site, and consumption. The linear correlation coefficient was r = 0.61 (Fig. 6). Given the uncertainty of crab consumption over the years and reported fishing sites, there is, except for a few subjects, remarkably good agreement between the two methods of estimating the intake.

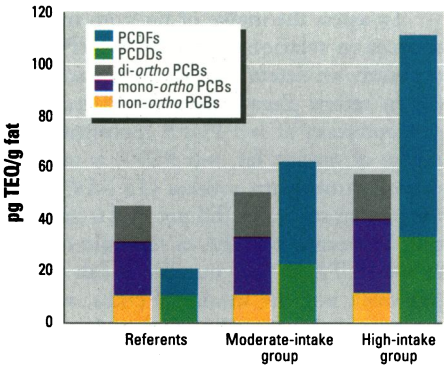

Figure 4. Mean blood concentrations (pg TEQs/g fat) of non-*ortho*-, mono-*ortho*- and di-*ortho*-PCBs, PCDDs, and PCDFs for the referents and the two crab-consuming groups.

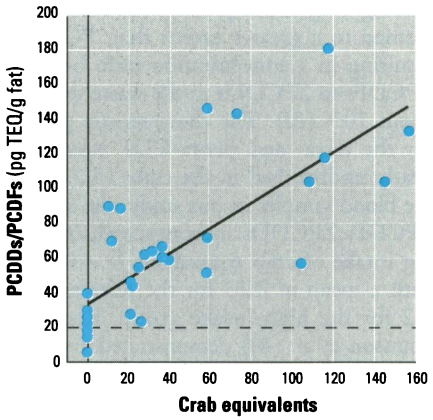

Figure 5. Relationship between intake of crab equivalents and blood concentrations of PCDDs and PCDFs (pg TEQ/g fat) in 34 subjects (r = 0.75).

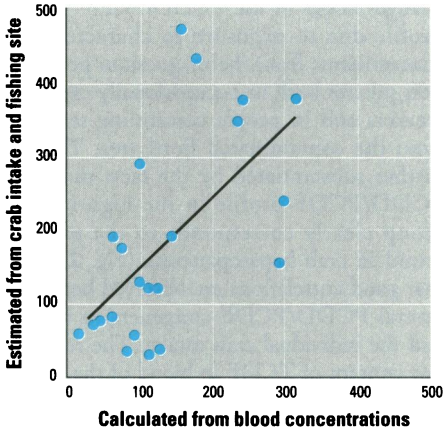

Figure 6. Relationship between estimates of PCDD/PCDF intakes (in ng TEQ/year) from crab consumption using either PCDD/PCDF blood concentrations or reported crab consumption and fishing site.

To assess the intake of fat from marine sources in relation to the PCDD/PCDF exposure, we determined the fatty acid profile in serum phospholipids. Whereas the concentration of *n*-3 PUFA represents the intake of marine fat, *n*-6 PUFA is mainly derived from plant sources (*12,42,43*). In the present study, we did not find a correlation between *n*-3 PUFA or the ratio of *n*-3 to *n*-6 PUFA and the number of fish meals per week nor the intake of crabs, which were mostly consumed more than 6 months before blood sampling. Consequently, we have not been able to find any correlation between the levels of *n*-3 PUFA and concentrations of PCDDs/PCDFs.

Discussion

During magnesium production, PCDFs are formed to a greater extent than PCDDS, resulting in a concentration ratio between ΣPCDFs to ΣPCDDs in the waste water of about 10:1 (*21*). The characteristic pattern for the tetra- and penta-CDF isomers is nearly undisturbed in the crabs (*5,21*). For the blood samples in our study, the ratio of ΣPCDFs:ΣPCDDs increases with increasing intake of crab equivalents (r = 0.699), with a mean of 0.13 for the referents and 1.2 for the high-intake group. Recently, Hansson et al. (*44*) demonstrated a similar increase of the ΣPCDFs:ΣPCDDs ratio in blood of workers from the same magnesium production plant with the number of years of employment in the plant giving a mean of 0.21 for the control group and 1.1 for the workers. This strongly indicates that changes occur in the PCDD/PCDF blood profile due to exposure to characteristic contaminants from the magnesium production process both in occupationally exposed workers and in people consuming seafood from the contaminated fjord area. This is further substantiated by the facts that the PCDD/PCDF profile in the high-intake group clearly corresponds to the profile found in crab hepatopancreas (Fig. 2) and that good correlations are observed between several PCDD/PCDF congeners in blood and the individual crab intake. The relative low content of TCDF in blood of the high-intake group could indicate that this congener has a shorter half-life.

In general, a high abundance of octa-CDD is observed in the fat fraction of human tissues, but its source has not yet been identified. Schecter et al. (*8*) reported octa-CDD ranging from 50% to 80% of the ΣPCDDs/PCDFs in blood samples from the general population living in different parts of the world. This corresponds well with the results of this study, where octa-CDD accounted for 74% of all PCDDs/PCDFs in the referents. In contrast, the relative contribution from octa-CDD was reduced to 32% for the high-consumer group due to the considerably higher concentrations of PCDFs in blood (Fig. 2), demonstrating the change in PCDD/PCDF profiles that follows crab consumption.

Levels of total PCDDs and PCDFs in our referents (563 and 73 pg/g fat) are comparable with mean concentrations of 461 and 85 pg/g fat for the control group of workplace exposure study of Hansson et al. (*44*) and with values of 489 and 53 pg/g fat reported in whole blood samples from Germany by Päpke et al. (*45*). Thus, the mean blood concentrations of PCDF found for our crab consumers (473 pg/g fat in the high-intake group) were clearly different from both Norwegian and German referents, but similar to those found in the magnesium plant workers (491 pg/g fat).

Previous studies from areas near the Baltic Sea with fish as a main source of dioxin exposure have reported strong correlations between blood levels of *n*-3 PUFA and dioxins as well as fish intake (*12,42,43*). In contrast, we did not find any association between *n*-3 PUFA and fish intake. This might be explained by the predominant consumption of lean fish in our study and the narrow range of fish intake (Table 1) in a relatively small population. Furthermore, the lack of a correlation between reported crab intake and *n*-3 PUFA is probably due to the limited season for crab consumption. Crabs are usually caught and consumed about 4 months a year, starting in August. The blood samples were collected in June, just before the crab season started. Because the half-lives of *n*-3 PUFA are quite short, an influence by former crab consumption on the *n*-3 PUFA concentrations is not expected. As a consequence, presuming that crab consumption is the main source of PCDD/PCDF exposure, no correlation was found between *n*-3 PUFA and PCDDs/PCDFs in blood.

Recently we reported on the congener-specific determination of PCBs in crabs from the Frierfjord area (*4*). Sum PCBs in the crabs, excluding PCB-209, was not much above background levels found in crabs from diffuse polluted areas along the coast [0.5–1 µg/g fat (*46*)]. However, the perchlorinated biphenyl PCB-209 showed a high abundance in the crabs, ranging from 2.9 to 0.05 µg fat in a gradient from fishing site A to F (*27,28*) (see Fig. 1). This congener has been identified as one of the major chlorinated components in the wastewater from the magnesium factory (*46*).

Surprisingly, the high concentrations of PCB-209 found in crabs from the Frierfjord area are not reflected in the blood of the crab consumers (Fig. 3; Table 3). This could be due to limited bioavailibility (*47*). Studies on mammals have shown that organochlorine compounds with a log *n*-octanol/water partition coefficient (log K_{ow}) >6.5 are poorly absorbed in the gastrointestinal tract (*47–50*). PCB-209, with a log K_{ow} of 9.6, is thus expected to have a low degree of absorption. Furthermore, the linear correlation coefficient between ΣPCDDs/PCDFs and ΣPCBs in the blood samples was low (r = 0.39). This fact and the similarity of PCB profiles for the referents and the high-intake group indicates that PCB exposure in our study group is only increased somewhat by crab consumption, but predominantly arises from other sources.

Blood concentrations of the major PCB congener, PCB–153 (189–554 ng/g fat in referents), as well as some other congeners (PCB-105, 118, 156 and 157), found in our study are in good agreement with the results obtained from control persons in a Swedish study [PCB-153, 220–760 ng/g fat for referents (*11*)]. On the other hand, our results for non-*ortho*-PCBs (PCB-126: 8–173 ng/g fat and PCB-169: 5–109 ng/g fat) seem to be considerably lower than for the Swedish nonconsumers of fish (PCB-126: 100-450 pg/g fat and PCB-169: 100-340 pg/g fat).

The calculated mean PCDD/PCDF exposure of the referents of 9.7 pg/kg body weight is in good agreement with an estimated intake of about 8–10 pg TEQ/kg body weight/week based on measurements of PCDDs/PCDFs in different food items in Norway (*51*). Consumption of contaminated crabs increases the total exposure to PCDDs/PCDFs considerably. The average total exposure calculated for the group with moderate crab consumption is with 31 pg/kg body weight, close to the tolerable weekly intake (TWI) (35 pg TEQ/kg body weight) proposed by a Nordic Expert Group (*30,52*), and only few subjects in this group exceeded this value. In contrast, nearly all subjects in the high-intake group exceeded the Nordic TWI. However, only two persons slightly exceeded the TWI of 70 pg TEQ/kg body weight recommended by a WHO expert group (*53*).

The use of the TEF concept for PCBs is controversial (*26*). However, based on measured concentrations in blood (see Fig. 4), PCBs in the referents would contribute twice as much as PCDDs/PCDFs to the total TEQs. In the moderate-intake group, PCBs and PCDDs/PCDFs would contribute equally to the total TEQs, whereas in the high-intake group PCDDs/PCDFs would contribute twice as much as the PCBs. With the inclusion of PCBs in the calculation of TEQs, the mean for the ref-

erents would be close to the Nordic TWI, whereas both groups of crab consumers would exceed the TWI.

Conclusion

The present study shows that among male recreational fishermen, consumption of crabs from the contaminated Frierfjord area is an important source of exposure to PCDDs/PCDFs. This is based on two findings: the PCDD/PCDF profile in blood of the high-intake group is clearly changed in the direction of that found in crabs from this area, and the measured blood concentrations of most PCDDs/PCDFs correlate strongly with the reported crab consumption and fishing site. No other major source of exposure to PCDDs/PCDFs could be identified through the questionnaire. It appears that the external exposure can be estimated both from reported consumption and fishing sites and from the PCDD/PCDF blood concentrations with fairly good agreement. Calculations of average weekly exposures from body burdens show that about half of the crab consumers exceeded the Nordic TWI of 35 pg TEQ/kg body weight/week, but only a few slightly exceeded the WHO TWI of 70 pg TEQ/kg body weight/week.

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